Unruptured cerebral aneurysms are considered a contraindication to intravenous tissue plasminogen activator for the treatment of acute ischemic stroke. This exclusion is due to the theoretical increased risk of intracranial hemorrhage (ICH) from aneurysm rupture postthrombolysis. This retrospective study sought to determine the safety of intravenous tissue plasminogen activator in this patient population. In their cohort, pre-existing cerebral aneurysms were found in 22 of 236 patients with prethrombolysis cerebrovascular imaging and postthrombolysis follow-up imaging. Three (14%) patients with pre-existing cerebral aneurysms developed intracranial hemorrhage, all of which were asymptomatic. The ICHs were mainly parenchymal and within the site of the cerebral infarct. In 2 of the patients, the hemorrhage occurred contralateral to the site of the cerebral aneurysm. The rate of postthrombolysis ICH in patients with pre-existing cerebral aneurysms (14%) was not significantly different from the rate of ICH among patients without aneurysms (19%). None of the patients with pre-existing aneurysms developed symptomatic ICH compared with 10 of the 214 patients (5%) without aneurysms. These findings suggest that intravenous tissue plasminogen activator is safe to administer to patients with pre-existing cerebral aneurysms because the rate of aneurysm rupture and symptomatic ICH is low. Although these results are quite encouraging and seem to suggest this population should not be excluded from administration of intravenous tissue plasminogen activator, the sample size in this study was low and thus further studies with larger cohorts are warranted before changing current practice. See p 412.

### Predictors of Tissue-Type Plasminogen Activator Nonresponders According to Location of Vessel Occlusion

Previous studies have shown that early artery recanalization is associated with good outcome after intravenous tissue plasminogen activator (IV tPA) in acute ischemic stroke. Recanalization with IV tPA, however, is achieved in 30% to 40% of patients and as such, catheter-based therapies have been developed for patients who fail IV tPA. Several factors such as clot burden have been shown to predict the likelihood of arterial recanalization. This prospective study investigated clinical and hemodynamic predictors of poor response to intravenous thrombolysis. Large vessel arterial occlusion was diagnosed with both carotid ultrasound and transcranial Doppler before IV tPA administration and assessment of recanalization was assessed by both tests 1 hour postthrombolysis. Five hundred forty-eight patients with intracranial occlusion were included and divided into 4 groups: proximal middle cerebral artery occlusion (n=251), distal middle cerebral artery occlusion (n=194), internal carotid artery T occlusion (n=61), and basilar artery occlusion (n=42). Recanalization during the first hour of tissue plasminogen activator was seen in 186 patients (33.9%); 107 (19.5%) had partial recanalization and 79 (14.4%) had complete recanalization. Recanalization was associated with good outcome at 3 months (43.1% modified Rankin Scale ≤2 versus 29.6% modified Rankin Scale ≥2, P=0.002). Among patients with proximal middle cerebral artery occlusion, the presence of severe extracranial internal carotid artery stenosis or occlusion and age ≥74 years independently predicted no recanalization to IV tPA. In patients with internal carotid artery T occlusion, history of hypertension and absence of atrial fibrillation were independent predictors of no recanalization. In patients with basilar artery occlusion, the absence of atrial fibrillation independently predicted no recanalization. This study is limited by its sample size and the use of transcranial Doppler, an operator-dependent imaging technique. However, the use of predictors of no recanalization after IV tPA and rapid neurovascular assessment may improve the selection of patients for more aggressive reperfusion strategies. Further study is needed to evaluate these findings. See p 417.

### Low-Molecular-Weight Heparin Versus Aspirin for Acute Ischemic Stroke With Large Artery Occlusive Disease: Subgroup Analyses From Fraxiparin in Stroke Study for the Treatment of Ischemic Stroke (FISS-Tris) Study

The Fraxiparin in Stroke Study for the treatment of ischemic stroke (FISS-Tris) study was a prospective, multicenter, randomized clinical trial that showed no superiority of nadroparin calcium, a low-molecular-weight heparin (LMWH), over aspirin for the primary end point (Barthel Index at 6 months) in patients with acute ischemic stroke and large artery occlusive disease. Patients were treated with either 0.4 mL nadroparin calcium 3800 antifactor Xa IU subcutaneously twice a day or 160 mg aspirin once a day within 48 hours of stroke onset for 10 days and subsequently patients were treated with 80 to 200 mg aspirin once daily for 6 months. The study in this month’s issue evaluates the efficacy of LMWH and aspirin in certain subgroups. Of the 353 patients with confirmed large artery occlusive disease, 300 had intracranial large artery occlusive disease only, 42 had both intracranial and extracranial, and 11 had only extracranial disease. Thus, a majority of patients had intracranial atherosclerotic disease. LMWH improved outcome compared with aspirin in patients >68 years of age (OR, 1.86; P=0.043). LMWH also improved the outcome in patients who were not on antiplatelet medications on admission (OR, 1.85; P=0.029). This result is in contrast to the Warfarin–Aspirin Symptomatic Intracranial Disease (WASID) study, in which there was no difference in recurrent stroke between warfarin and aspirin in patients on or off antithrombotic medications at enrollment. A major difference, however, between these trials was that in WASID, the median time from qualifying event to randomization was 17 days, whereas in the FISS-tris study, LMWH was started within 48 hours, and thus the initiation of LMWH at an earlier stage may improve outcome in this subgroup. LMWH also improved outcome in patients with symptomatic posterior circulation disease (OR, 5.76; P=0.001). These findings suggest that LMWH may be of benefit in certain subgroups of patients with acute stroke and large artery occlusive disease. It is unclear, however, why the LMWH group had better outcome in these subgroups. In the initial FISS-tris study (Lancet Neurol, 2007), there was no significant difference in the occurrence of thromboembolic events (such as recurrent stroke, acute coronary syndrome, deep vein thrombosis, and pulmonary embolus) between the LMWH and aspirin groups. Data regarding thromboembolic events were not provided in this subgroup analysis. Based on the preliminary results of the Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis (SAMMPRIS) trial, which showed promising results of dual antiplatelet therapy with aspirin and clopidogrel in the treatments of symptomatic intracranial atherosclerotic disease, perhaps further study is warranted to compare LMWH or other novel anticoagulants with dual antiplatelet therapy in intracranial large artery disease. See p 346.
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